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(English translation of the amended sheets of the IPER)

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Claims

1. A method for the detection of small quantities of particles by the detection of antigen-
5 antibody precipitates which comprises:
providing a sample fluid that essentially contains particles with a given maximum particle
size, the particles having at least two antibody binding sites;
providing a fluid containing antibodies that essentially contains particles having a given
maximum particle size;
10 contacting the sample fluid with the fluid containing the antibodies, which yields a reaction
fluid where in the presence of particles having at least two antibody binding sites the
antibodies can form an antigen-antibody precipitate;
directing a light beam through the reaction fluid;
detecting a signal by measuring with a photodetector the extinction at the light-dark boundary
15 of the cone of light that is produced when the light generated by the laser is passing through
the measuring cell containing the reaction fluid, the signal strength depending on the size and
number of antigen-antibody precipitates formed.
2. A method according to claim 1, wherein the method has a detection sensitivity going down to
20 the femtomolar or attomolar range.
3. A method according to any of the preceding claims, wherein the step of providing a sample
fluid that essentially contains particles having a given maximum particle size comprises:
25 a) providing a fluid,
introducing a sample into the fluid, and
separating particles that exceed a given particle size, in order to obtain a sample fluid that
essentially contains only particles having a given maximum particle size, or
b) providing a fluid that essentially contains particles having a given maximum particle size

and

introducing a sample into the fluid that essentially contains particles having a given maximum particle size, in order to obtain a sample fluid that essentially contains particles having a given maximum particle size.

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4. A method according to any of the preceding claims, wherein the separation of the particles having a size exceeding the given maximum particle size is effected by filtration, the filter having a pore size of preferably 20 – 450 nm, more preferably of 100 – 300 nm, and particularly of 200 nm.

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5. A method according to any of the preceding claims, wherein at least two monoclonal antibodies or one polyclonal antibody are employed as antibodies.

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6. A method according to any of the preceding claims, wherein the antibody is selected from the group consisting of immunoglobulin G or immunoglobulin M.

7. A method according to any of the preceding claims, wherein the method allows the quantity of particles to be detected quantitatively or semiquantitatively.

- 20 8. A method according to any of the preceding claims, wherein, at a constant concentration of antibodies, the decrease of the measured signal is directly related to the concentration of antigens.

- 25 9. A computer program product comprising program code means stored in a computer readable medium, for carrying out the method according to any of the claims 1 to 8 when the computer program product is executed on a computer, a network device or a device, particularly an analytical detection device.

- 30 10. A computer program product comprising a program code downloadable from a server, for carrying out the method according to any of claims 1 to 8 when the computer program product is executed on a computer, a network device or a device, particularly an analytical detection device.

11. A kit for qualitative and/or quantitative detection of a given particle to be detected, wherein the given particle has at least two antibody binding sites, the kit comprising:
- at least one antibody that is capable of specifically binding to the given particle, and
- 5 at least one suitable fluid for receiving the sample, and
- a device for the detection of small quantities of particles comprising:
- a laser,
- a measuring cell, and
- a photodetector designed for carrying out a measurement of extinction at the light-dark
- 10 boundary of the cone of light that is produced when the light generated by the laser is passing through the measuring cell containing the particles in a fluid.

antibody-complex having a lower solubility in the solvent used than the antigen and antibody used, which reaction at first results in turbidity of the reaction mixture and, subsequently, in sedimentation of this antigen-antibody-complex.

The method according to the invention allows small quantities of particles to be detected. For example, by using the method according to the invention, a limit of detection in the range of femtograms and attograms per liter could be achieved with low-molecular-weight substances, i. e., with substances having a molecular weight of less than 500 g/mol, whereas up to now, the detection limit usually is in the range of micrograms, nanograms, or picograms per liter. The limit of detection is higher with substances having a molecular weight in the range above 500 g/mol, for example, the limit of detection is about 300 femtograms/liter with substances having a molecular weight of 150,000 g/mol (e. g., IgG antibodies). This means that the sample fluid may contain particles in an order of magnitude of femtomoles or attomoles per liter.

In a first partial step of the method according to the invention, a sample fluid is provided that essentially contains particles having a given maximum particle size. There are, for example, two ways to achieve this. According to a first option, initially a fluid is provided that essentially contains only particles having a given maximum particle size, and subsequently, a sample that essentially contains particles having a given maximum particle size is added to the fluid. According to a second option, the sample fluid can be obtained by initially providing a fluid, adding a sample to the fluid and, subsequently, removing particles that exceed a given particle size.

The maximum particle size of the particles in the sample fluid and in the other fluids that essentially contain only particles of a given maximum particle size can be selected depending on the desired application. With many common antibodies, particles may be separated that are larger than 20 – 450 nm, more preferably larger than 100 – 300 nm, and particularly larger than 200 nm. This separation can